LAW OFFICES OF JONATHAN ALAN QUINE

Tracie Brooks

Attorney Docket No. 02-031910US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Juha Punnonen, et al.

Application No.: 09/886,942

Filed: June 21, 2001

NOVEL CHIMERIC PROMOTERS

Examiner: Unassigned

Art Unit: 1645

LETTER TO OFFICIAL DRAFTSPERSON

Attn: Box Missing Parts

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

For:

Applicant hereby submits 23 sheets of formal drawings to be made of record in the above-identified case.

Respectfully submitted,

Emily M. Haliday, J.D., Phyt

Reg. No. 38,903

LAW OFFICES OF JONATHAN ALAN QUINE P.O. BOX 458 Alameda, CA 94501 (510) 337-7871

Fax (510) 337-7877

Figure 1: Screening libraries of chimeric promoter sequences

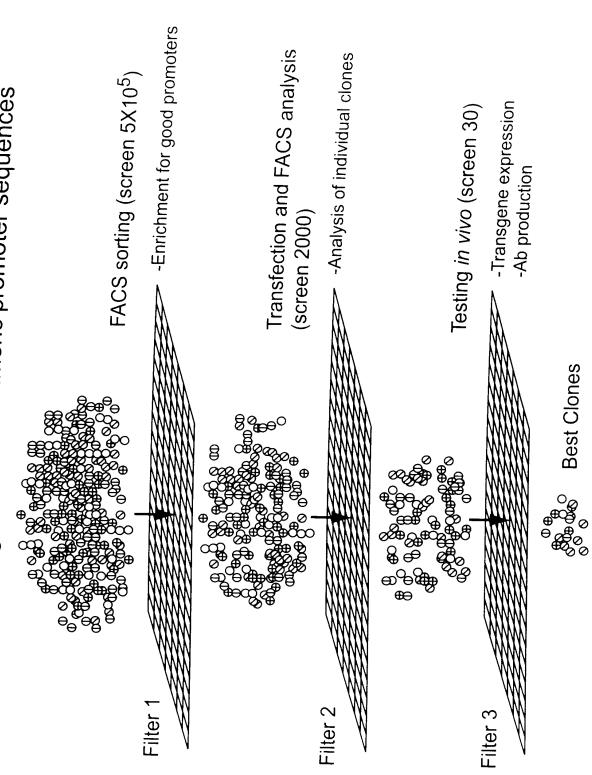
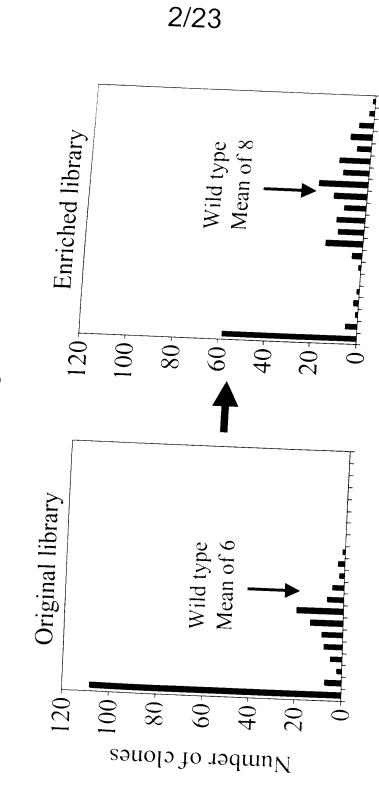


Figure 2: Enrichment of chimeric promoter libraries by FACS sorting



Reporter gene expression

Figure 3: Diverse activities of chimeric promoter sequences in transfected cells

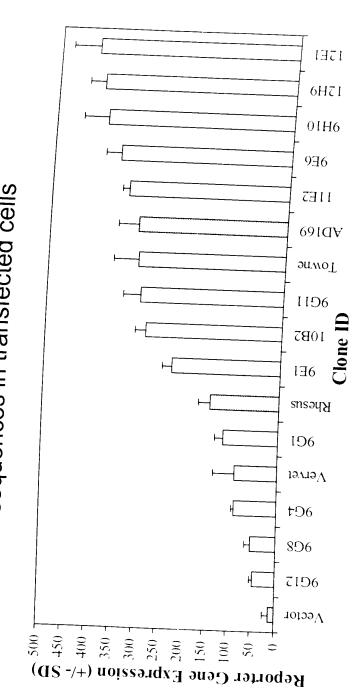


Figure 4: Luciferase expression in muscle 7 days after plasmid injection

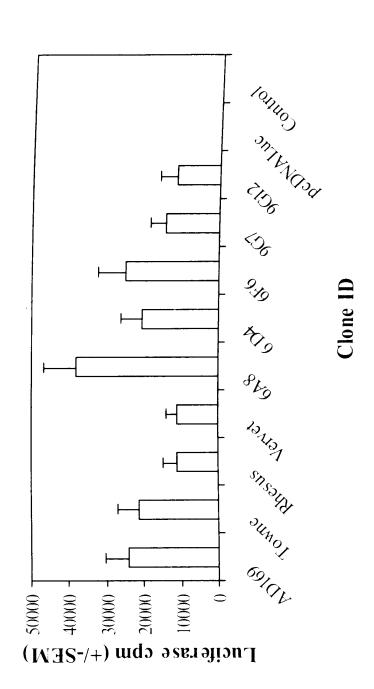


Figure 5: Comparison of Luciferase expression from clone

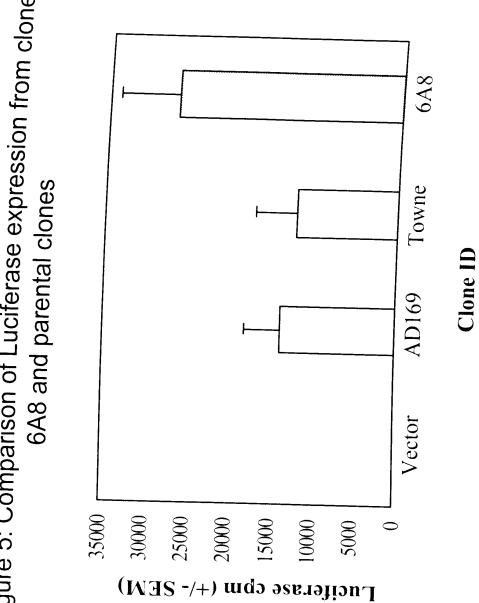
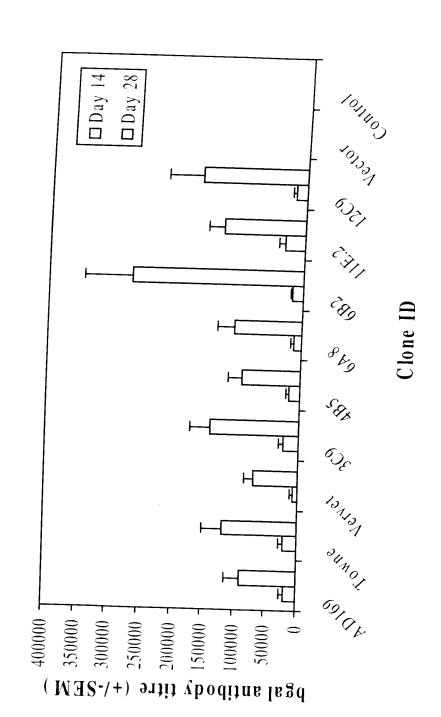


Figure 6A: Antibody responses following injection with β galactosidase-encoding plasmid



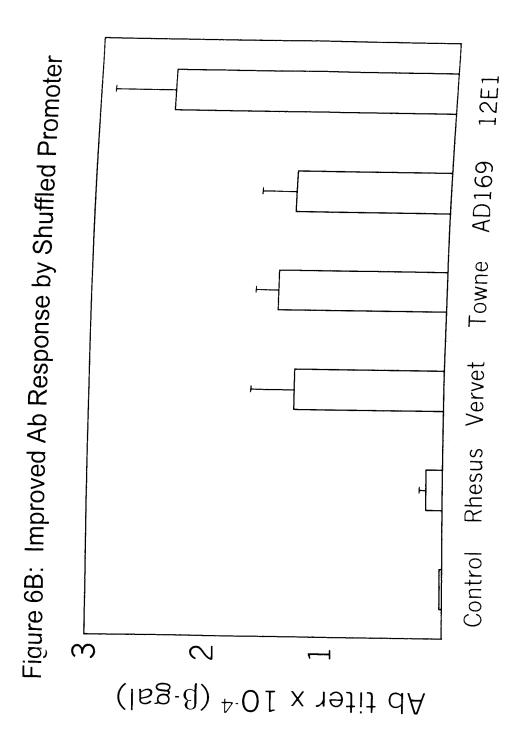


Figure 7: Chimeric promoter 6A8 is functional in human muscle tissue

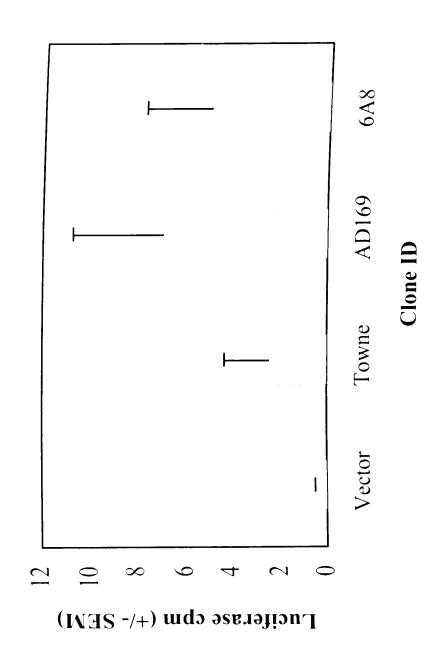


Figure 8A: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

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ATATUAGGCTATATCGCCGATAGAGGCGACATCAAGCTGGCACATGGCCAATGCATATCGATCTATACATTAAATCAATATTGGCAATTAGCCATATTTG
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Figure 8B: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences

Figure 8C: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

```
gacgicaatgggtggagtatitacggtaaactgcccacttggcagtacatcaagtgtatcatatgccaagtccg-cccctattgacgtcaatgacgta
                                                                                                              GACGTCAATGGGTGTGTTTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTCCG-CCCCTATTGACGTCAATGACGTTA
                                                     GACGTCAATGGGTGGAGTATTTACGGTAAACTGCTCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACG-CCCCCTATTGACGTCAATGACGGTA
                                                                                                                                                                    GACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAGGTGTATCATATGCCAAGTACG-CCCCCTATTGACGTCAATGACGTA
                                                                                                                                                                                                                                                                                   GACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTCCGCCCCCTATTGACGTCAATGACGTA
                                                                                                                                                                                                                                                                                                                                                                                              GACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTCCG-CCCCTATTGACGTCAATGACGTA
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                                                                                                                                                                                                                                                                                                                                                                                                                                                   GACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATATCATATGCCAAGTCCG-CCCCCTATTGACGTCAATGACGGTA
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6F6
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Figure 8D: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 AATCAACGGGACTTTCCAAAATGTCGTAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGG AGGTCTATATAAGCAGAGTTT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              AATUAAUGGGACTTTCCAAAATGTCGTAATAACCCCGCCCGTTGACGCAAATGGGCGGTAGGTGTGTACGGTGGGAGGTCTATATAAGTAAATTAAGTAAAT
                                                                                                                                                                                                                     GITTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTTGTTTTTGGTTAAAA
                                                                                                                                                                                                                                                                                                      GTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTTGACTCACGGGGGATTTCCAAGTCTCCACCCATTGACGTCAATGGGAGTTTTGTTTTTGGCAGT
                                                                                                                                                                                          AATCAACGGGACTTTCCAAAATGTCGTAATAACCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAAATGTCTTTC
                                                                                                                                                                                                                                                                                                                                                                                        AATCAACGGGACTTTCCAAAATGTCGTAATAACCCCGCCCCGTTGAAAATGGGCGGTAGGCGTGTACGGTGGGGAGGTCTATATAAGCAAGTTCCATT
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                                                                                            GTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAAATGGGGG-
                                                                                                                                                                             GITTIGGCAGIACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGG
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                   from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.
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Figure 8E: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

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TAGTGAACCGCCATTCTGCCTGGGGACGT-----CGGAG----GAGCACCAT-AGAAGGTACCGGGACCGATCCAGCCTCCATAGCCGGGAACGGTGCA
TAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCAT-AGAAGACACCGGGACCGATCCAGCCTCCGCGGCGGGAACGGTGCA
                      TAGGGAACCGCCATTCTGCCTGGGGACGC-----CGGAG----GAGCTCCATTGGAAGAGCCGGGACCGATCCAGCCTCCGCGGCCGGGACGGTGCA
                                              TAGGGAACCGCCATTCTGCCTGGGGACGC-----CGGAG----GAGCACCAT-AGAAGACACCGGGACCGATCCAGCCTCCATAGCCGGGACGGTGCA
                                                                     TAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCAT-AGAAGACACCGGGACCGATCCAGCCTCCGCGGGACCGGGAACGGTGCA
                                                                                             TAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCAT-AGAAGACACCGGGACCGATCCAGCCTCCGCGGCCGGGACGGTGCA
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Figure 8F: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

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CITGGGGTCTATACACCCCCGCTTCCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGTTATTGACCATTATTGACCACTCCCTATTGG
                                                                                                                                              CTTGGGGGCCTATACACCCCCGCTTCCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGGTTATTGACCATTATTGACCACTCCCCTATTGG
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                             CTTGGGGCCTATACACCCCCCCCCCTTCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGTTATTGACCATTATTGACCATCCCCCTATTGG
                                                                                       CTTGGGGTCTATACACCCCCCGCTTCCTTATGCTATAGGTGATGGTATAGCTTAGCCTATAGGTGTGGGTTATTGACCATTATTGACCACTCCCCTATTGG
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Figure 8G: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

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TCTGTATTTTTACAGGATGGGGTCTCATTTATTATTACAAATTCACATATACAACGCGGCGGTCCCCCGTGCCGGCGGTTTTTATTAAACATAGCGTGG
TCTGTATTTTTACAGGATGGGGTCCCATTTATTTACAAATTCACATATACAACACCACCGTCCCCAGGTGCCCGCAGTTTTTGTTAAACATAGCGTGG
                                                                                                TCTGTATTTTACAGGATGGGGTCCCATTTATTACAAATTCACATATACAACACCACCGTCCCCAGTGCCCGCAGTTTTTATTATAAACATAGCGTGG
                                                                                                                                                                                                        TCTGTATTTTACAGGATGGGGTCCCATTTATTATTACAAATTCACATATACAACAACGCCGTCCCCCGTGCTCGCAGTTTTTATTAAACATAGCGTGG
                                                                                                                                     TCTGTATTTTACAGGATGGGGTCTCATTTATTACAAATTCACATATACAACACGCGTCCCCCGTGCCGGAGTTTTTATTAAACATAGGGTGG
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Figure 8H: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences rom AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

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TCATGGTCGCTCCGCCAGCTCCTTGCTCCTAACAGTGGAGGCCAGACTTAGGCACGACGACGACGACCACCACCACCAGCAGTGTGCCGCACAAGGCCGTTGGCGG
                                                                                                                                             TCATGGTCGCTCGGCAGCTCCTTGCTCCCAACAGTGGAGGCCAGACTTAGGCACAGGAGGATGCCCACCACCACCAGTGTGCCGCACAAGGCCGTGGCGG
                                                                                                                                                                 TCATGGTCGCTCGGCAGCTCCTTGCTCCTAACAGTGGAGGCCAGACTTAGGCACACAGTGCCCACCACCACCACCACGTGTGCCGCACAAGGCCGTGGCGG
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                    TCATGGTCGCTCGGCAGCTCCTTGCTCCTAACAGTGGAGGCCAGACTTATGCACAGACACAATGCCCACCACCACCACCAGTGTGCCGCACAAAGGCCGTGGCGG
                                                                                  TCATGGTCGCTCGGCAGCTCCTTGCTCCTAACAGTGGAGGCCAGACTTATGCACAGCACAATGCCCACCACCACCACAGTGTGCCGCACAAGGCCGTGGCGG
                                                                                                     TCATGGTCGCTCGGCAGCTCCTTGCTCCCAACAGTGGAGGCCAGACTTAGGCACAGCACAATGCCCACCACCACCACAGTGTGCCGCACAAGGCCGTGACGG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              TAGGGTATGTGTCTGAAAATGAGCTCGGAGATTGGGCTCGCACCGCTGACGCAGATGGAAGACTTAAGGCAGCGGCAGAAGAAGAAGAAGAAGCAGCTGAGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  TAGGGTATGTGTCTGAAAATGAGCTCGGAGATTGGGCTCGCACCGCTGACGCAGATGGAAGACTTAAGGCAGGGGCAGAAGAAGAAGAAGAAGAAGGCAGCTGAGT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     TAGGGTATGTGTCTGAAAATGAGCTCGGAGATTGGGCTCGCACCGCTGACGCAGATGGAAGGACGTTAAAGGCAGCGGCAGAAGAAGAAGAAGTGCAGCAGCTGAGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    TCATGGTCGCTCGTGCTCCTTGCTCCTAACAGTGGAGGCAGACTTAGGCCACAATGCCCACCACCACCACGAGGCGCACAAGGCCGTTGCTGCGCACAAGGCCGTTGCTG
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Figure 81: Comparison of 18 chimeric promoter sequences generated by DNA shuffling using CMV promoter nucleic acid sequences from AD169 and Towne human strains and Rhesus and Vervet monkey strains as parental sequences.

Vector for premoter evolution

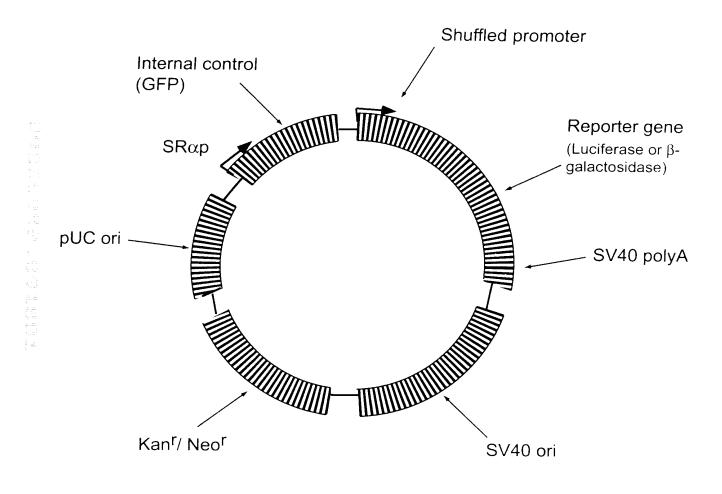


Fig. 9

Figure 10A

	19	9/23	
1 ATATGAGGCTATATCGCCGATAGAGGCGACATCAAGCTGGCACATGGCCAATGCAT ACTTGGCACGGTGCCAA.GTTTGGGGCGGGGTCTTGGCACCGTGCCAA ATTGAATTGGCATGGTGCCAATAATGGCGGCCATATTGGCTATATGCCA	120 ATCGATCTATACATTGGAATTTGGCAATTAGCCATATTAGTCATTGGTTATATAGCGTCCGCCATATTGGTTTTGGCATATGTCCAATATTATTGATCCATATAGC	121 ATAAATCAATATTGGCTATTGGCCATTGCATACGTTGTATCTATATCATAATATGTACAT CAATATCCAATATGGCTAATAGCCA	181 TTATATTGGCTCATGTCCAATATGACCGCCATGTTGACATTGATTATTCACTAGTTAT CAATATGCCATTGGCCAA.TGGCAA.TGGGCCAGTATTGATTATAGCCAATATAT ATGCCATATAGTATTCCATATATGGGTTTTCCTATTGACGTAGATAGCCCCTCCCAAT
Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq

Figure 10B

		20	0/23	
241	TAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCCATATATGGAGTTCCGC AGGCAATAATCCATATTGGCATATGTCCATATTGCCTATACCCATATTGGC GGGCGGTCCCATATACCATATATGGGGCTTCCTAATACCGCCCATAGCCCCCC	301 GTTACATAACTTACGGTAAATGGCCCGCCTCGTGACCGCCCAACGACCCCCCGCCC TTATGTCCATTACCAATACCATATATGGGTCTTCCTATATACGTCATAGGTACCGCCC ATTGACGTCAATGGTCTCTATATAGGTCTTTCCTATTGACGTCATAGGTACCGCCC	361 ATTGACGTCAA ATTGACGTAATATGGATACGCCTCCATTGACGTCAATGGGAGGGA	421 TAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCA TAATACCGCCCATTGACGTGTATAGGACCGTCCCATTGACGTCAATAGGCCCACCTCCCA TCAATGCCCATTGACGT
	Towne_promoter_ir_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq

Figure 10C

481	TTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTAC TTGACGTCAATGGGGTGGCCCATTGCCCATTC	600 ATCAAGTGTATCATATGCCAAGTCCGGCCCCCTATTGACGTCAATGACGGTAAATGGCCC	660 GCCTGGCATTATGCCCAGTACATGACCTTACGGGACTTTCCTACTTGGCAGTACATCT	661	ACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTTGGCAGTACACCAA ACCTATTAATAGTAACTTGGCAAGTAAATGGGTACTTGGCAGTACACCAAGG.TACAT ATCTATTAATAGTAACTTGGCAAGTACATTACTATTGGCAAGTACGCCAAGG.TACAT
	Towne_promoter_ir_PCR_prod_seg Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seg	Towne_promoter_fr_PCR_prod_seq_Rhesus_monkey_PCR_prod_821bp_Vervet_(Simian)_PCR_product_seq_	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq		Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq

Figure 10D

	721
Towne_promoter_ir_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp /ervet_(Simian)_PCR_product_seq	
Towne_promoter_fr_PCR_prod_seq_Rhesus_monkey_PCR_prod_821bp_ervet_(S'mian)_PCR_product_seq_	781CACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTTCATGCCC.ATTGACGTCAATGGGG
Towne_promoter_ir_PCR_prod_seq_Rhesus_monkey_PCR_prod_821bp_Pervet_(Simian)_PCR_product_seq_	841 AAATGTCGTAATAACCCCGCCCCGTTGACGCAAATGGGCG
Towne promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp /ervet (Simian) PCR product seq	901 GTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCG GTAGGCGTGC.CTATGGGCGGTCTATATAAGCAATGCACGTTTAGGGAACCGCCATTCTG GTAGGCGTGCCTAATGGGAGGTCTATATAAGCAATGCTCGTTTAGGGAACCGCCATTCTG

SEQ TO NO:23

Figure 10E

1020 CGGG.ACCGATCCAG CGGGGACCGATCCAG	SEQ ID NO:20 SEQ ID NO:22
961 CCTGGAGACGCCATCCACGCTGTTTTGACCTCCAT.AGAAGACACCGGG.ACCGATCCAG CCTGGGGACGTCGGAGGAGCACCAT.AGAAGGTACCGGGGACCGATCCAG CCTGGGGACGTCGGAGGAGCTCCATTGGAAGAAGACCGGG.ACCGATCCAG	1021 CCTCCGCGGCCGGGAACGGTGCATTGGAACGCGGATT CCTCCATAGCCGGGAAGGGTGCATTGGAACGCGGATA CCTCCATAGCCGGGACGGTGCATTGGAATGCGGATA
Towne_promoter_ir_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq	Towne_promoter_fr_PCR_prod_seq Rhesus_monkey_PCR_prod_821bp Vervet_(Simian)_PCR_product_seq